UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/695,578	10/27/2003	Scott A. Waldman	08321-0157 CT1	5382

35148 7590 08/31/2006

COZEN O' CONNOR, P.C..
1900 MARKET STREET
PHILADELPHIA, PA 19103-3508

EXAMINER	
AEDER, SEAN E	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 08/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/695,578	WALDMAN, SCOTT A.	
	Examiner	Art Unit	
	Sean E. Aeder, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

The response filed on 7/28/06 to the restriction requirement of 6/26/06 has been received. Applicant has elected Group V, claims 24-25, for examination. Because Applicant did not distinctly and specifically point out any errors in the restriction requirement, the election has been treated as an election without traverse (MPEP 818.03(a)).

Claims 1-25 were pending.

Claims 1-23 were cancelled by Applicant.

Claims 24-25 were amended by Applicant.

Claims 26-46 were newly added by Applicant

Claims 24-46 are currently under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 24-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 24-29, 36-39, and dependent claims 30-35 and 40-46 are rejected as vague and indefinite because claims 24-29 and 36-39 recite the term "human ST receptor protein" as the sole means of identifying the polynucleotides of the claimed method. The use of laboratory designations only to identify a particular molecule

renders the claims indefinite because different laboratories may use the same laboratory designations to define completely distinct molecules. Amending the claims to specifically and uniquely identify human ST receptor protein by SEQ ID NO can obviate the rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24-27, 30-37, 40-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the claims are inclusive of a genus of polynucleotides comprising a nucleic acid that encodes an epitope of human ST receptor protein. However, the written description in this case only sets forth a polynucleotide encoding full-length human ST receptor protein (SEQ ID NO:1). The specification does not disclose identify any other polynucleotides comprising a nucleic acid encoding an epitope of human ST receptor protein as broadly encompassed in the claims.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common to that genus that "constitute a substantial portion of the

genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus."

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., F.3d, 2004 WL 260813, at *9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genus. That is, the specification provides neither a representative number of polynucleotide sequences that encompass the genus of polynucleotides comprising a nucleic acid that encodes an epitope of human ST receptor protein nor does it provide a description of structural features that are common to polynucleotides comprising a nucleic acid that encodes an epitope of human ST receptor protein. Although the specification prophetically states that epitopes "are generally at least 6-8 amino acids in length" (page 11 lines 30, in particular), the specification does not identify a single epitope. Further, Roitt et al (Immunology, 1993, 3rd ed, Mosby, London) teaches that although it is possible to produce antibodies to almost any part of an antigen, this does not normally happen in an immune response. It is usually found that only certain areas of the antigen are particularly antigenic, and that a majority of antibodies bind to these regions. Said regions are often at exposed areas on the

outside of an antigen, particularly where there are loops of polypeptide that lack a rigid tertiary structure (pages 7.7-7.8, in particular). This is exemplified by Holmes (Exp. Opin. Invest. Drugs, 2001, 10(3):511-519) which teaches that rabbits were immunized with synthetic peptides which in each case generated high anti-peptide specific immunoreactivities, however, none of the antibodies exhibited binding to the full length antigen. The author concludes that "presumably, expression of these epitopes in the context of the protein was important and affected the antibody binding ability (page 513 column 1). Since the specification has not identified which polynucleotides encode polypeptides characteristic of human ST receptor protein epitopes, one could not predict which polynucleotides encode polypeptides characteristic of human ST receptor protein epitopes. Further, determining which polynucleotides encode polypeptides that function as epitopes for the human ST receptor protein would, in itself, require undue experimentation. Since the disclosure fails to describe common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of a polynucleotide encoding full-length human ST receptor protein (SEQ ID NO:1) is insufficient to describe the genus. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The

specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolation. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only a polynucleotide encoding full-length human ST receptor protein (SEQ ID NO:1), but not the full breadth of the claims, meets the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 24-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to

which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re* Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. See also *Ex parte* Forman, 230 USPQ 546 (BPAI 1986).

The claims are broadly drawn to a method of treating an individual who has metastasized colorectal cancer or an individual who is susceptible to metastasized colorectal cancer with an immunotherapeutic vaccine comprising a nucleic acid molecule encoding at least one epitope of human ST receptor protein.

The specification prophetically describes methods of treating an individual who has metastasized colorectal cancer or an individual who is susceptible to metastasized colorectal cancer with a vaccine comprising a nucleic acid molecule encoding at least one epitope of human ST receptor protein (page 11-12, in particular). However, the specification lacks working examples using a vaccine comprising a nucleic acid

molecule encoding at least one epitope of human ST receptor protein to treat any individual.

Therapeutic treatments, in general, are unpredictable. With regards to tumor immunotherapy, the goal of tumor vaccination is the induction of tumor immunity to prevent tumor recurrence and to eliminate residual disease. However, gene therapy against tumors is highly unpredictable as underscored by Crystal, R.G. (Science, Vol. 270, October 1995, pages 404-410) who teaches that in tumor vaccine studies intended to evoke a tumor-directed immune response, there is no convicining evidence (other than anecdotal case reports) that tumors actually regress, despite the promising observations in experimental animals. In other words, humans are not simply large mice (page 409, 1st column). More recently, Tait *et al.* (Clin.Canc.Res., Vol. 5, July 1999, pages 1708-1714) revealed just how unpredictable gene therapy was in the clinical setting. The authors' prior phase I trial of 12 patients with extensive ovarian cancer treated with a retroviral vector expressing the BRCA1 splice variant (LXSN-BRCA1sv) demonsrated vector stability, minimal immune response, gene transfer and expression, and some tumor reduction in the patients (page 1708, 2nd column, 2nd paragraph). In contrast, the Phase II trial inititiated in pateints with stage III and IV grade ovarian cancer, showed a high preponderance for vector instability (vector was degraded rapidly), a rapid immunological response invoking neutralizing antibodies to the retroviral vector, and no clinical response to the therapy. Although the difference in response to the therapy may be attributed to differences in immunocompetence between the phase I and II patients (page 1712, 2nd column), the end result seems to

indicate that further experimentation is necessary prior to the successful application of DNA vaccines, especially with the regards to cancer therapy. Further, therapeutic cancer treatments, in general, are unpredictable, as underscored by Gura (Science, 1997, 278:1041-1042.) who discusses the potential shortcoming of potential anti-cancer agents including extrapolating from in-vitro to in-vivo protocols, the problems of drug testing in knockout mice, and problems associated with cologenic assays. Indeed, since formal screening began in 1955, thousands of drugs have shown activity in either cell or animal models, but only 39 that are used exclusively for chemotherapy, as opposed to supportive care, have won approval from the FDA (page 1041 first column, in particular) wherein the fundamental problem in drug discovery for cancer is that the model systems are not predictive.

Further, those of ordinary skill in the art recognize that treatment in vivo is not predictive. The instant situation is analogous to that of *In re* Brana (34 U.S.P.Q. 2d 1436, 1440 (Fed. Cir. 1995)). A review of *In re Brana* reveals an application that claimed a chemical compound for treating a cancer, wherein the chemical compound was structurally similar to known compounds that have known in vivo use to treat tumors, and more importantly, Applicant provided in vivo data that the claimed compound could treat tumors in mice, hence it was ruled that the claimed compound was enabled for treating tumors. In the instant application, the claim is not drawn to a vaccine comprising a nucleic acid molecule encoding at least one epitope of human ST receptor protein which has known in vivo ability to give rise to a therapeutic effect. Further, the instant specification provides no in vivo data, particularly demonstrating that

the claimed vaccine would predictably give rise to a therapeutic effect in vivo. In view of *In re Brana*, Examiner asserts that successful use of in vivo mouse models of colon cancer enables compositions for specific therapeutic effects in humans and does not require human clinical testing; however, the instant application is claiming a vaccine that provides a therapeutic effect without providing any in vivo data, hence the claimed invention is not enabled. All of this underscores the criticality of providing workable examples which are not disclosed in the specification, particularly in an unpredictable art, such as vaccine treatment.

In view of the teachings above and the lack of predictability, guidance, workable examples and or exemplification in the specification, it would require undue experimentation by one of skill in the art to make the invention.

Summary

No claim is allowed. Claims 24-46 are rejected under 35 U.S.C. 112, first paragraph, but free of the prior art teaching a method of treating an individual who has metastasized colorectal cancer or an individual who is susceptible to metastasized colorectal cancer with an immunotherapeutic vaccine comprising a nucleic acid molecule encoding at least one epitope of human ST receptor protein. The closest prior art for claims 24-46 is Almenoff et al (Journal of Biological Chemistry, 1994, 24(17): 16610-16617), which teaches the human ST receptor protein (page 16611, in particular); however, this reference does not teach or suggest a method of treating an individual who has metastasized colorectal cancer or an individual who is susceptible to

metastasized colorectal cancer with an immunotherapeutic vaccine comprising a nucleic acid molecule encoding at least one epitope of human ST receptor protein.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean E. Aeder, Ph.D. whose telephone number is 571-272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SEA

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER